R E M A R K S

Claim Amendments

Claims 1 and 5 were amended to recite the latanoprost concentration that was previously recited in claims 9 and 10.

Editorial revisions were also made to claims 1 and 5.

Claim 4 was amended to depend on claim 1.

Claim 8 was amended to depend on claim 5.

Claims 9 and 10 were canceled.

With respect of 37 CFR 1.116, entry of the amendments is respectfully requested, since the amendments involve features that were set forth in the claims prior to the final rejection.

Rejection Under 35 USC 103

Claims 1, 4, 5 and 8 to 10 were rejected under 35 USC 103 as being unpatentable over Dean et al. (USP 6,166,073) in view of The Patent Abstract of Japan and Hellberg et al. (USP 6,646,001) for the reasons set forth on page 2 of the July 25, 2008 Office Action.

It was admitted in the November 16, 2008 Office Action that Dean et al. do not teach tonicity agents such as glycerin, polyethylene glycol, propylene glycol, mannitol, trehalose or sucrose.

Presently Claimed Invention

The present inventors first confirmed the problem of white turbidity due to a change of formulation (complex formation - see the paragraph bridging pages 3 and 4 of the present specification) in ophthalmic solutions containing latanoprost at a certain concentration (0.005% (W/V)) and benzalkonium chloride ("BAK") at a certain concentration (0/003 to 0.01% (W/V)), and then discovered the following means to solve the problem:

1) using BAK represented by the formula of $[C_6H_5CH_2N(CH_3)_2R]$ C1 (wherein R is an alkyl group having 12 carbon atoms) as the preservative, and/or

2) adding a tonicity agent consisting essentially of a nonionic tonicity agent.

As described in the present specification, white turbidity, which is a problem that is solved by the presently claimed invention, is observed in the case where latanoprost at the above-mentioned concentration and BAK at

the above-mentioned concentration exist in the solutions, and is not observed under conditions other than the above (see page 3, line 13 to page 4, line 7 of the present specification).

Cited References

Dean et al. (USP 6,166,073) describe compositions containing a DP-agonist and a FP-agonist prostaglandin agonist for treating glaucoma or ocular hypertension. However, Dean et al. do not teach or suggest ophthalmic solutions containing latanoprost and benzalkonium chloride ,wherein both have concentrations where white turbidity is observed. From this fact, it is respectfully submitted that one of ordinary skill in the art would not recognize from Dean et al. the problem to be solved by the presently claimed invention or the solution to the problem, which is provided by the presently claimed invention.

The patent Abstract of Japan does not describe or suggest latanoprost.

Hellberg et al. (USP 6,646,001) describe compositions for the treatment of glaucoma and ocular hypertension, comprising a prostaglandin FP receptor agonist and a prostaglandin synthesis inhibitor. However, Hellberg et

al. do not teach or suggest ophthalmic solutions containing latanoprost and benzalkonium chloride, wherein both have concentrations where white turbidity is observed. From this fact, it is respectfully submitted that a person of ordinary skill in the art would not recognize from Hellberg et al. the problem to be solved by the presently claimed invention or the solution to the problem, which is provided by the presently claimed invention.

As discussed above, an ophthalmic solution containing latanoprost having the above-mentioned concentration and BAK having the above-mentioned concentration is not described in any of the cited references. Therefore, a person of ordinary skill in the art would not recognize the problem solved by the presently claimed invention from any of the cited references, alone or combined. Accordingly, the presently claimed invention is not taught or suggested by cited references, either alone or combined.

Advantageous Results of the Presently Claimed Invention

It was contended at the middle of page 2 of the July 25, 2008 Office Action that the data in the present specification, i.e., one concentration of latanoprost

(0.005%) and two concentrations of BAK (0.01% and 0.005%), is not commensurate in scope with the claims.

In reply to the aforesaid contention, submitted concomitantly herewith is a DECLARATION UNDER 37 CFR 1.132 of Hiroyuki ASADA dated January 20, 2009 showing the results of the experiments.

Consideration of the enclosed January 20, 2009 ASADA DECLARATION is respectfully requested, since it is in response to the Examiner's comments in the final rejection.

Table 1 on page 18 of the present specification and Table 5 on page 24 of the present specification show that white turbidity in a latanoprost ophthalmic solution is observed in the case where the concentration of BAK is 0.01% or 0.005%. In the enclosed January 20, 2009 ASADA DECLARATION, additional experiments were carried out following the same procedure as in Experiment 1-1) of the present specification for the case where the concentration of BAK is 0.0075 or 0.003%. The following Table (a) shows the results.

Table (a)

	Comparative formulation A-1	Comparative formulation A-2
Latanoprost	0.005	0.005
Crystalline sodium dihydrogenphosphate	0.2	0.2
Sodium chloride	0.9	0.9
BAK	0.007	0.003
Diluted hydrochloric	q.s.	q.s.
Sodium hydroxide	q.s.	q.s.
Purified water	q.s.	q.s.
Appearance	White turbidity	Slightly white turbidity

(Unit in Table: % (W/V), q.s.: quantum sufficient)

Tables 1 and 5 and Table (a) reveal that white turbidity was observed in a latanoprost-containing ophthalmic solution containing BAK having a concentration of 0.01%, 0.007%, 0.005%, or 0.003%.

Table 3 on page 20 of the present specification and Table 7 on page 25 of the present specification show that white turbidity in a latanoprost ophthalmic solution is prevented by replacing BAK (0.01% and 0.0005%) with BAK- C_{12} (0.01% and 0.0005%). In the enclosed January 20, 2009 ASADA DECLARTION, additional experiments were carried out following the same procedure as in Experiment 1-3) of the present specification for the case where the concentration of BAK-C_{12} is 0.007% or 0.003%. The following Table (b) shows the results.

Table (b)

	Formulation B-1	Formulation B-2
Latanoprost	0.005	0.005
Crystalline sodium dihydrogenphosphate	0.2	0.2
Sodium chloride	0.9	0.9
BAK-C_{12}	0.007	0.003
Diluted hydrochloric	q.s.	q.s.
Sodium hydroxide	q.s.	q.s.
Purified water	q.s.	q.s.
Appearance	Colorless and Transparent	Colorless and transparent

(Unit in Table: % (W/V), q.s.: quantum sufficient)

Tables 3 and 7 and Table (b) show that a latanoprost-containing ophthalmic solution containing BAK-C_{12} having a concentration of 0.01%, 0.007%, 0.005%, or 0.003% was colorless and transparent.

Table 4 on page 21 of the present specification and Table 8 on page 26 of the present specification show that white turbidity in a latanoprost-containing ophthalmic solution is prevented by adding to the solution one of concentrated glycerin, mannitol, PEG 400, propylene glycol and trehalose, which are all nonionic tonicity agents, in the case where the concentration of BAK is 0.01%. In the enclosed January 20, 2009 ASADA DECLARATION, additional experiments were carried out following the same procedure as in Experiment 1-4) of the present specification for the

case where the concentration of BAK is 0.007%. The following Table (c) shows the results.

Table (c)

	Formulation C-1	Formulation C-2	Formulation C-3	Formulation C-4	Formulation C-5
Latanoprost	0.005	0.005	0.005	0.005	0.005
Crystalline sodium dihydrogenphosphate	0.2	0.2	0.2	0.2	0.2
BAK	0.007	0.007	0.007	0.007	0.007
Concentrated glycerin	2.5				
Mannitol		5			
PEG 400			8.5		
Propylene glycol				2.1	
Trehalose					9.25
Diluted hydrochloric acid	q.s.	q.s.	q.s.	q.s.	q.s.
Sodium hydroxide	q.s.	q.s.	q.s.	q.s.	q.s.
Purified water	q.s.	q.s.	q.s.	q.s.	q.s.
Appearance	Colorless and transparent	Colorless and Transparent	Almost colorless and transparent	Colorless and transparent	Colorless and transparent

(Unit in Table: % (W/V), q.s.: quantum sufficient)

Tables 4 and 8 and Table (c) show that a latanoprost-containing ophthalmic solution was colorless and transparent in the case where the concentration of BAK is

0.01% or 0.007%, and one of concentrated glycerin, mannitol, PEG 400, propylene glycol, and trehalose, which are nonionic tonicity agents, is added.

It is respectfully submitted that the above-mentioned experiments provide test data that is commensurate in scope with applicants' present claims which recite a concentration range of BAK of 0.003% to 0.01% (W/V) and a concentration range of BAK-C_{12} of 0.003% to 0.01% (W/V.

Withdrawal of the 35 USC 103 rejection is respectfully requested.

Reconsideration is requested. Allowance is solicited.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

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Respectfully submitted,

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Encs.: (1) PETITION FOR EXTENSION OF TIME; (2) NOTICE OF APPEAL; (3) DECLARATION UNDER 37 CFR 1.132 of Hiroyuki ASADA dated January 20, 2009